Movement Disorders
CLINICAL PRACTICE

REVIEW

Effects of Deep Brain Stimulation on Postural Trunk Deformities: A Systematic Review

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ABSTRACT: Background: Deep brain stimulation (DBS) effects on postural deformities are still poorly explored.
Methods: Systematic review in accord with the Preferred Reporting Items for Systematic review and Meta-Analysis guidelines (PRISMA).
Results: All 38 studies that met predefined eligibility criteria had high risk of bias attributed to retrospective analysis of heterogeneous populations with variable and incompletely reported demographic and clinical characteristics, definitions, outcomes, DBS indications, targets, and settings. Five patient groups were identified in the 35 studies with individual data available: (1) parkinsonian camptocormia (n = 96): 89 patients underwent subthalamic (STN) and 7 globus pallidus pars interna (GPi) DBS. Camptocormia was the indication in 3 patients. After DBS, camptocormia improved in 57 of 96 patients (4.3–100% improvement) and remained stable or worsened in 39 of 96 patients (2–100% worsening). (2) dystonic camptocormia (n = 16): All underwent GPi-DBS. They were younger and with shorter disease duration, but longer deformity duration, compared with parkinsonian camptocormia. After GPi-DBS, camptocormia improved in all patients (50–100% improvement). (3) Parkinsonian Pisa syndrome (n = 14): 11 patients underwent STN-DBS for motor fluctuations whereas Pisa syndrome was the indication for pedunculopontine and GPi-DBS in 2 patients. After DBS, Pisa improved in 10 of 14 patients (33.3–66.7% improvement). (4) Dystonic opisthotonus: 2 young patients remarkably responded to GPi-DBS. (5) Parkinsonian anterocollis: There were variable responses in 3 patients after STN-DBS for motor fluctuations.
Conclusions: Low-quality level of evidence suggests that dystonic camptocormia and opisthotonus improve after GPi-DBS. Parkinsonian camptocormia, Pisa syndrome, and anterocollis have variable responses, and their dystonic features should be further explored.

Axial postural deformities include trunk anteroflexion (camptocormia), lateroflexion (Pisa syndrome), retroflexion (opisthotonus), and neck anteroflexion (anterocollis), which often complicate Parkinson's disease (PD).[1–3] The pathogenesis and pathophysiology of these deformities most likely involve multifactorial central and peripheral mechanisms that are potentially different, depending on the underlying disease process (e.g., PD vs. dystonic syndromes). Though these deformities are relatively uncommon, they are difficult to treat and their progression is associated with significant disability, particularly in patients with PD.[1–3] Reported effects of deep brain stimulation (DBS) on postural trunk deformities have varied from significant worsening to remarkable improvement. The aim of this systematic review is to evaluate the quality of evidence and summarize the effectiveness and/or harms of DBS for the management of postural trunk deformities.

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Methods

Registration

Protocol development and preliminary literature review began March 1, 2018. In accord with the Preferred Reporting Items for Systematic review and Meta-Analysis guidelines (PRISMA),[4,5] the protocol for this systematic review and meta-analysis (if appropriate) was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on April 5, 2019 (CRD42019131176).

Search Strategy

Literature search strategies were developed combining medical subject headings (MeSH) and other terms related to DBS and postural trunk deformities: "deep brain stimulation," "brain stimulation," and "neuromodulation" and the singular and plural forms of "trunk," "trunk deformity," "axial deformity," "trunk myopathy," "spine deformity," "postural deformity," "stooped posture," "camptocormia," "kyphosis," "hyperkyphosis," "bent spine," "bent spine syndrome," "opisthotonus," "Pisa," "Pisa syndrome," "pleurothotonus," "scoliosis," "antecollis," "anterocollis," "dropped head," "dropped head syndrome," "chin on chest syndrome," "neck extensor myopathy," and "camptocephalia." Search filters were not used, and there were no language, timing, or setting restrictions.

Information Sources

We searched the following databases biweekly between March 1, 2018 and July 7, 2019: MEDLINE (OVID interface, 1948 to present), EMBASE (OVID interface, 1980 to present), PsycINFO, Global Health, Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register, Health Technology Assessment Database, Web of Science (Science and Social Science Citation Index), and Google Scholar. Additionally, the International Clinical Trials Registry Platform Search Portal and ClinicalTrials.org were searched for ongoing or recently completed trials, and PROSPERO was searched for similar ongoing or recently completed systematic reviews. To ensure literature saturation, we scanned the reference lists of included studies and relevant reviews for additional relevant cited and citing articles. We also searched our personal files to make sure all relevant material was captured. The search was updated toward the end of the review.

Eligibility Criteria

Studies were selected according to the following criteria:

- Design: any study or publication type.
- Participants: adult human population (aged ≥18 years) with the following postural deformities: trunk anteflexion (camptocormia) and/or lateroflexion (Pisa syndrome) and/or retroflexion (opisthotonus) and/or dropped head syndrome (anterocollis) regardless of the underlying neurological condition.
- Intervention: DBS, regardless of the anatomical target.
- Comparators: status before DBS (if available).
- Outcomes: (1) Presence or absence of postural deformity after DBS; (2) percentage change in the corresponding postural angle after DBS (or any other outcome measure utilized in the study).
- Exclusion criteria: postural deformity associated with tardive syndromes, idiopathic cervical dystonia, or segmental craniocervical dystonia, including Meige syndrome.

Selection Process

The authors independently assessed the risk of bias in included studies by considering randomization, allocation concealment, blinding, data completeness, selective outcome reporting, and other potential sources of bias (Fig. 1). Disagreements were resolved by discussion with involvement of a senior faculty from our institution, when necessary. See Tables 1–3 for information regarding risk of bias in each individual study included in this systematic review.

Data Extraction, Collection, and Analysis

Individual patient data were extracted from selected articles and synthetized using predefined data extraction forms based on the above-mentioned criteria and preliminary literature review. Before formal article review, a calibration exercise was undertaken to pilot and refine specific information to be extracted. The predefined templates were used to build four summary tables

(Tables 1–4). During data extraction, we juxtaposed authors and institutions in order to prevent double-counting information (e.g., case report republished as case series). We contacted

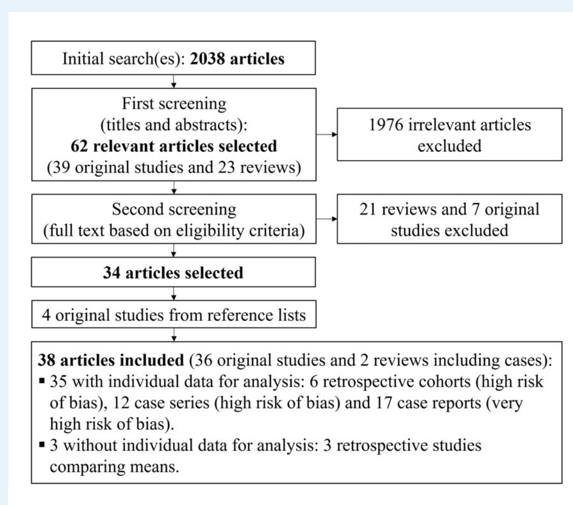

FIG. 1. Diagram depicting the literature review and article selection process for this systematic review.

TABLE 1 *Summary of studies for patients with Parkinsonian camptocormia treated with DBS*

Ref.	Study Design (Sample Size, Risk of Bias)	Median Age (Years), Sex	Median Disease Duration (Years)	Median Deformity Duration (Months)	L-Dopa Response	Paraspinal Myopathy	DBS Target	Outcome Measures	Median Change Post-DBS	Median Follow-up Time (Months)
6	Retrosp. cohort (3, high)	NR	NR	NR	NR	NR	BL STN	T angle for upper campto-cormia	T angle 49.1° to 42.3° (13.8% better)	NR
								TL angle for lower campto-cormia	TL angle 36.4° to 18.9° (48.1% better)	
7	Retrosp. cohort (23 campto-cormia +5 Pisa, high)	NR	NR	NR	NR	NR	BL STN	UPDRS-III-28	2.46 to 1.71 points (30.5% better)	NR
8	Retrosp. cohort (29, high)	64.5 ± 1.2 15F/14M	11.8 ± 0.9	NR	Yes = 16 No = 3 NR = 10	NR	BL STN	C7SVA	>5 cm better in 17 pts. (NR)	NR
9	Retrosp. cohort (17, high)	66, 10F/7M	11	40	Yes = 14 No = 3	NR	BL STN	TL angle	59° to 45° (23.7% better)	34
10	Retrosp. cohort (14, high)	67, 6F/8M	13.5	48	NR	No = 9 Yes = 5	BL STN	TL angle	60° to 35° (41.7% better)	6
11	Retrosp. cohort (25, high)	67, 4F/21M	14	27	No	NR	BL STN = 24, BL STN + GPi = 1	TL angle	45° to 30° (33.3% better)	30.9
12	Case series (3, high)	65, 3M	12	NR	No	NR	BL STN = 2, BL GPi = 1[1]	BFMDRS-trunk	9 to 6 points (33.3% better)	16
13	Case series (4, high)	61, 2F/2M	12	72	NR	No = 3 Yes = 1	BL STN	TL angle	45° to 25.5° (43.3% better)	22.5
14	Case series (8, high)	63, 6F/2M	17	NR	Yes = 6 No = 2	NR	BL STN	UPDRS-III-28	2 to 1.5 points (25% better)	12
15	Case series (6, high)	51, 4F/2M	9.5	25	NR	NR	BL STN	TL angle	75° to 10° (86.7% better)	16.5
20	Case series (3, high)	68, NR	22	47 (developed after DBS)	No	Yes	BL STN	TL angle	NR	NR
21	Case series (2, high)	63, 2M	21	36	NR	Yes	BL STN	Clinical observ. (NR)	Same or worse (NR)	12
22	Case series (2, very high) (P)	62.5, 2F	12.5	84	NR	NR	BL GPi	Clinical observ. (NR)	Same or worse = 1, better = 1 (NR)	15
23	Case series (2, high)	59, 2M	NR	NR	Yes = 1 NR = 1	NR	BL STN = 1, BL GPi = 1	Clinical observ. (NR)	Same or worse (NR)	19.5
34	Case report (very high)	57, F	13	60	No	No	BL GPi[1]	Shoulder-hip-knee angle	133° to 160° (20.3% better)	12
35	Case report (very high)	62, F	14	48	No	NR	BL STN	Clinical observ. (NR)	Same or worse (NR)	24
36	Case report (very high)	58, M	7	24	Yes	NR	BL STN[1]	Clinical observ. (TL angle)	45° to 0° (100% better)	3
37	Case report (very high)	62, F	21	120	No	NR	BL STN	TL angle	60° to 10° (83.3% better)	6

(Continues)

TABLE 1 *Continued*

Ref.	Study Design (Sample Size, Risk of Bias)	Median Age (Years), Sex	Median Disease Duration (Years)	Median Deformity Duration (Months)	L-Dopa Response	Paraspinal Myopathy	DBS Target	Outcome Measures	Median Change Post-DBS	Median Follow-up Time (Months)
38	Case report (very high)	63, F	19	12	No	NR	BL STN	TL angle	80° to 20° (75% better)	60
39	Case report (very high)	NR, F	NR	NR (developed after DBS)	NR	Yes	BL STN	Clinical observ. (NR)	Worse (NR)	NR
40	Case report (very high)	53, M	25	228	No	NR	BL STN	Clinical observ. (TL angle)	90° to 0° (100% better)	10
41	Case report (very high)	71, F	11	60	No	NR	BL STN	Clinical observ. (TL angle)	90° to 15° (83.3% better)	20
42	Case report (very high)	62, M	10	18	No	NR	BL GPi	Clinical observ. (TL angle)	45° to 10° (77.8% better)	14
44	Case report (very high)	NR, NR	NR	NR	NR	NR	BL STN	Clinical observ. (NR)	Same or worse (NR)	NR

[1] DBS performed to treat camptocormia.

BFMDRS-trunk, trunk subscore of the Burke-Fahn-Marsden Dystonia Rating Scale; BL, bilateral; C7SVA, C7 sagittal vertical axis; F, female; GPi, globus pallidus pars interna; L-Dopa, levodopa; M, male; NR, not reported; observ., observation; P, poster; prosp., prospective; ref., reference; restrosp., retrospective; STN, subthalamic nucleus; T, thoracic; TL, thoracolumbar; UPDRS-III-28, question 28 of part III of the Unified Parkinson's Disease Rating Scale.

TABLE 2 *Summary of studies for patients with dystonic camptocormia and opisthotonus treated with DBS*

Ref	Study Design (Sample Size, Risk of Bias)	Median Age (Years), Sex	Median Disease Duration (Years)	Median Deformity Duration (Months)	L-Dopa Response	Paraspinal Myopathy	DBS Target	Outcome Measures	Median Change Post-DBS	Median Follow-up Time (Months)
					Dystonic camptocormia					
12	Case series (4, high)	54.5, 2F/2M	14	NR	No = 3 NR = 1	Yes = 1 NR = 3	BL GPi	BFMDRS-trunk	12 to 4.5 (62.5% better)	15
16	Case series (3, high)	54, 2F/1M	2	24	No = 1 NR = 2	NR	BL GPi	BFMDRS-trunk	5.3 to 0.7 (88.9% better)	39
17	Case series (2, high)	60 (NR = 1) 1F/1M	7	84	NR	No	BL GPi	BFMDRS-trunk	16 to 3 (81.3% better)	18
18	Case series (2, high)	23.5, 1F/1M	1.75	21	NR	No	BL GPi	Clinical observ. (TL angle)	90 to 0 (100% better)	43
19	Case series (3, high)	46, 3M	4	48	NR	NR	BL GPi	Clinical observ. (NR)	Better (NR)	48 (NR = 2)
22	Case report (very high) (P)	67, M	10	120	NR	No	BL GPi	TL angle	90 to 0 (100% better)	60
31	Case report (very high)	42, M	5	36	No	NR	BL GPi	BFMDRS-trunk	16 to 8 (50% better)	15
					Dystonic opisthotonus					
32	Case report (very high)	29, M	20	216	NR	NR	BL GPi	Clinical observ. (NR)	Better (NR)	4
33	Case report (very high)	25, M	11	108	NR	NR	BL GPi	BFMDRS-trunk	12 to 2 (83.3% better)	24

BFMDRS-trunk, trunk subscore of the Burke-Fahn-Marsden Dystonia Rating Scale; BL, bilateral; F, female; GPi, globus pallidus pars interna; L-Dopa, levodopa; M, male; NR, not reported; observ., observation; P, poster; ref., reference; TL, thoracolumbar.

TABLE 3 *Summary of studies for patients with Parkinsonian Pisa syndrome and anterocollis treated with DBS*

Ref	Study Design (Sample Size, Risk of Bias)	Median Age (Years), Sex	Median Disease Duration (Years)	Median Deformity Duration (Months)	L-Dopa Response	Paraspinal Myopathy	DBS Target	Outcome Measures	Median Change Post-DBS	Median Follow-up Time (Months)
	Parkinsonian Pisa syndrome									
6	Retrosp. cohort (2, high)	NR	NR	NR	NR	NR	BL STN	Lateral TL angle	16.9° to 5.5° (67.5% better)	NR
7	Retrosp. cohort (5 Pisa +23 campto-cormia, high)	NR	NR	NR	NR	NR	BL STN	UPDRS-III-28	2.46 to 1.71 points (30.5% better)	NR
14	Case series (10, high)	65, 8F/2M	11.5	NR	No = 6 Yes = 4	NR	BL STN	UPDRS-III-28	Better = 7 (50%) Same = 3	12
24	Case report (very high)	73, M	7	24	No	NR	BL GPi	Lateral TL angle	45 to 25° (44.4% better)	48
25	Case report (very high)	69, M	27	6 (developed after DBS)	No	NR	BL STN	Lateral TL angle	12 to 4° after CL voltage reduction (66.7% better)	15
26	Case report (very high)	69, M	8	12	No	NR	Right PPN	Lateral TL angle	52 to 30° (42% better)	40
27	Case report (very high)	62, F	6	12	NR	NR	Left PPN	Clinical observ. (NR)	Better (NR)	14
	Parkinsonian anterocollis									
28	Case report (very high)	60, F	15	1	No	NR	BL STN	Clinical observ. (NR)	Same (NR)	NR
29	Case report (very high)	50, M	12	132	No	Yes	BL STN	Clinical observ. (NR)	Same (NR)	NR
30	Case report (very high)	54, F	10	60	No	No	BL STN	Clinical observ. (NR)	Better (NR)	6

BL, bilateral; CL, contralateral; F, female; GPi, globus pallidus pars interna; L-Dopa, levodopa; M, male; NR, not reported; observ., observation; PPN, pedunculopontine nucleus; ref., reference; STN, subthalamic nucleus; TL, thoracolumbar; UPDRS-III-28, question 28 of part III of the Unified Parkinson's Disease Rating Scale.

corresponding study authors to resolve any uncertainties or missing data.

Given that there is no minimum clinically important difference reported for any postural abnormality and given that previous meta-analytic comparisons have been performed using improvement thresholds of 50% or > 15 degrees, we decided to dichotomize absolute individual postural deformity outcomes as "improved" or "not improved." We then calculated the percentages of postsurgical changes (improvement or worsening) for the corresponding outcome measures and assessed the data for further meta-analytic or statistical comparisons, if possible and appropriate.

Results

A total of 2,038 articles were screened by reading titles and abstracts. Thirty-nine original articles and 23 reviews were selected for full-text review and screening based on the eligibility criteria outlined above. Thirty-two original articles (seven excluded), four additional articles found in reference lists, and two reviews that included case reports met inclusion criteria. Thus, a total of 38 articles were selected for data extraction (Fig. 1).[6–43] Full data are available from the authors upon request.

High Risk of Bias: Retrospective Design, Variable Population, and No Control Group

All 38 original studies that met predefined eligibility criteria are observational and retrospective (i.e., nonrandomized and lacking a control group). Three of these studies are retrospective cohorts with relatively large samples of 74 to 158 PD patients. These three studies report comparisons of pre- and postsurgical means, but individual patient data are not available.[6–8] Of the remaining 35 articles, there were three additional retrospective cohort studies,[9–11] 12 case series with sample sizes of up to 25 patients,[12–23] and 20 case reports.[24–43]

Thirty-one studies evaluated the effects of DBS on postural deformities in PD patients. One study reported postural abnormalities after withdrawal of dopaminergic medications.[9] The other 30 studies retrospectively analyzed postural deformities during the best medication and stimulation conditions. Four case reports evaluated Pisa syndrome,[24–27] and three case reports assessed anterocollis in PD.[28–30] One study reported both camptocormia and Pisa syndrome in PD.[14] There were no reported PD patients with opisthotonus.

Nine studies assessed the effects of DBS in dystonia patients with postural deformities: five reported camptocormia,[16–19,31] and two reported opisthotonus.[32,33] There were no reported dystonia patients with Pisa syndrome. Two studies reporting camptocormia included both PD and dystonia patients.[12,22]

TABLE 4 *Comparative summary of outcome measures for patients with postural deformities treated with DBS*

		Postsurgical Improvement in Outcome Measure										
		All Outcomes		Postural Angle[1]		Clinical Observation		UPDRS-III Item 28		BFMDRS Item Trunk		
Presurgical Postural Deformity	DBS Target	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Total Cases
Parkinsonian camptocormia	BL STN	53	36	44	26	3	6	5	3	1	1	89
	BL GPi	4	2	1	0	2	2	–	–	1	0	6
	BL STN + GPi	0	1	0	1	–	–	–	–	–	–	1
Dystonic camptocormia	BL GPi	16	0	1	0	5	0	–	–	10	0	16
Parkinsonian Pisa syndrome	BL STN	7	4	0	1	–	–	7	3	–	–	11
	UL PPN	2	0	1	0	1	0	–	–	–	–	2
	BL GPi	1	0	1	0	–	–	–	–	–	–	1
Dystonic opisthotonus	BL GPi	2	0	–	–	1	0	–	–	1	0	2
Parkinsonian anterocollis	BL STN	1	2	–	–	1	2	–	–	–	–	3

Sample sizes not large enough to perform statistical comparisons.
[1] Thoracolumbar or shoulder-hip-knee angle for camptocormia; lateral thoracolumbar angle for Pisa syndrome.
BL, bilateral; GPi, globus pallidus pars interna, PPN, pedunculopontine nucleus; STN, subthalamic nucleus; UL, unilateral.

Variability in Terminology, Definitions, and Outcomes

Camptocormia (trunk anteflexion, bent spine syndrome) was defined using a thoracolumbar or bending angle threshold of either ≥30[10,11] or ≥ 45 degrees.[8,9] One case report used the shoulder-hip-knee angle.[34] Ventral thoracolumbar angle ≥30 degrees and ventral thoracic angle ≥45 degrees were used to define lower and upper subtypes of camptocormia, respectively.[6] These subtypes were also investigated in another study.[9] Scoliosis was defined as a Cobb angle >15 degrees in one article.[8] Yet, most studies that reported scoliosis did not include predefined thresholds.

Pisa syndrome (trunk lateroflexion) was more consistently defined as lateral thoracolumbar angle ≥10 degrees.[6,7] Anterocollis (neck anteflexion, camptocephalia, and dropped head syndrome) was defined using a threshold angle of 45 degrees.[6] In another study, x-rays were used to define anterocollis as a C7 sagittal vertical axis > 5 cm.[8] There was no reported definition for opisthotonus (trunk retroflexion, ectatocormia).[32,33] Methods to determine postural angles were also variable and included patient pictures, video frames, x-rays, CT studies, and/or computer software specifically designed for this purpose in one recent study.[6]

Regarding coexisting postural abnormalities, one report specified that patients with both camptocormia and lateroflexion would be excluded.[10] The rest of the studies either did not specify or acknowledged some degree of trunk lateroflexion along with camptocormia.

Outcome measures were also variable. Most articles reported postural abnormalities as qualitative clinical observations.[18,19,21–23,27–30,32,35–43] Some of them provided figure(s) and/or video(s) allowing for a semiquantitative estimation of the corresponding postural angles.[23,27,36–38,40–42] The most common quantitative outcomes reported for camptocormia were the changes in thoracolumbar angles,[6,9–11,13,15,22] item 28 of part III of the Unified Parkinson's Disease Rating Scale (UPDRS-III),[6,7,14] trunk item of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS),[12,16,17,31] a composite camptocormia score,[20] and shoulder-hip-knee angles.[34] Quantitative outcomes for Pisa syndrome were the change in lateral thoracolumbar angle[24–26] and the UPDRS-III item 28.[14] The only quantitative measure reported for opisthotonus was the trunk item of the BFMDRS.[33] Anterocollis outcomes were based on clinical observation only.[28–30] A recent study evaluated changes in global postural angles after subthalamic DBS (STN-DBS), regardless of the presence or absence of postural abnormalities.[6] When reported, postsurgical follow-up times were also variable: 3 to 67 months for camptocormia, 12 to 48 months for Pisa syndrome, 4 to 24 months for opisthotonus, and 6 to 9 months for anterocollis.

Variability in Demographic and Clinical Characteristics

Most studies reported age, sex, diagnosis, presurgical disease, postural deformity duration, and postsurgical follow-up duration. Other presurgical features were inconsistently reported and included upper versus lower camptocormia subtypes, coexisting postural abnormalities, levodopa responsiveness of the postural abnormality, presurgical evidence for paraspinal truncal or cervical myopathy (clinical, electrodiagnostic, imaging, and/or pathological), evidence for truncal or cervical spine deformities, and postsurgical levodopa equivalent daily dose reduction.

Variability in DBS Indications, Anatomical Targets, and Settings

All studies consistently reported DBS targets: bilateral STN only (18 studies), bilateral globus pallidus pars interna (GPi) only (2 studies),[34,42] and bilateral STN and/or GPi (4 studies)[11,12,22,23] for PD patients with camptocormia; bilateral GPi for dystonia patients with camptocormia (7 studies); bilateral STN (2 studies),[14,25] unilateral pedunculopontine (PPN; 2 studies),[26,27] and bilateral GPi (1 study)[24] for PD patients with Pisa syndrome; and bilateral GPi for the dystonia patients with opisthotonus (2 studies) and bilateral STN for the PD patients with anterocollis (3 studies). Remarkably, reported postural deformities developed after DBS implantation in three studies.[20,25,39]

In almost all studies reporting on PD patients, the DBS indication was either motor fluctuations or not specified. Camptocormia was the indication for bilateral STN-DBS in 1 patient and for bilateral GPi-DBS in 2 PD patients.[12,34,36] In all studies reporting on dystonia patients, the indication for bilateral GPi-DBS was camptocormia. Regarding studies reporting Pisa syndrome in PD patients, the indication for bilateral STN-DBS was motor fluctuations,[14,25] the indication for bilateral GPi-DBS was Pisa syndrome,[24] and the indication for unilateral PPN-DBS was either Pisa syndrome or severe postural instability.[26,27] The indication for bilateral GPi-DBS in the two articles reporting opisthotonus in dystonia patients was the opisthotonus itself.[32,33] For the three studies reporting PD patients with anterocollis, the indication for bilateral STN-DBS was motor fluctuations.[28–30] DBS parameters were significantly variable across the studies.

Semiquantitative Analysis and Summary

After evaluating the data for sample size, heterogeneity, and risk of bias, we concluded that available data did not meet criteria for a random-effect meta-analysis to pool mean differences and standard errors of outcomes. Given that the application of meta-analytic techniques would not be appropriate for the low-quality level of evidence available, the significant study heterogeneity, and variability described above,[44] we decided to semiquantitatively analyze and summarize the available evidence.

Parkinsonian Camptocormia

Extracted data for Parkinsonian camptocormia is summarized in Table 1. A total of 154 PD patients treated with DBS had presurgical camptocormia, and 4 additional PD patients developed camptocormia after bilateral STN-DBS.[20,39] Three relatively large retrospective reports comparing postural angle means before and after STN-DBS included 62 patients with presurgical deformities.[6–8] In the largest of these studies, 3 of 158 PD patients (1.9%) treated for motor fluctuations with STN-DBS had presurgical camptocormia. Two of them had lower camptocormia, their ventral thoracolumbar angle improved 48.1%, and camptocormia disappeared after STN-DBS. In the third patient, upper camptocormia persisted despite the ventral thoracic angle improving 13.8%.[6] In another relatively large report based on x-ray studies, 29 of 74 PD patients (39.2%) treated with STN-DBS for motor fluctuations had presurgical, levodopa-responsive lower camptocormia. The C7SVA improved >5 cm in 17 of these 29 patients (58.6%). This study also reported Cobb angle improvement of >5 degrees after STN-DBS in 5 of 13 patients (38.5%) with presurgical scoliosis.[8] In the third of these studies, 23 of 101 PD patients (22.8%) were reported as having camptocormia and 5 Pisa syndrome (4.9%). After combining both groups, 64.3% of them improved, 32.1% remained stable, and 3.6% worsened after STN-DBS based on item 28 of the UPDRS-III.[7]

Individual data were available for 96 PD patients with camptocormia (52 men, 40 women, and 4 not reported). Median presurgical PD duration was 13 years, and median presurgical camptocormia duration was 38 months. Median age at DBS surgery was 64 years. Seven patients had upper camptocormia, 22 lower camptocormia, 1 both, and 66 were undetermined. Seven patients had pure camptocormia, and 7 had camptocormia plus other postural abnormalities (4 Pisa syndrome, 2 anterocollis, and 1 bent knees). Coexistence of postural abnormalities was not specified in 82 patients.

Camptocormia was levodopa responsive in 22 patients (22.9%), not levodopa responsive in 43 patients (44.8%), and not specified in 31 patients. Trunk paraspinal myopathy was evidenced in 12 patients (12.5%), not evidenced in 13 patients (13.5%), and not reported in 71 patients. Spinal bone deformities were evidenced in 4 patients (4.2%), not evidenced in 11 patients (11.5%), and not reported in 81 patients.

The DBS target was the bilateral STN in 89 patients, bilateral GPi in 6 patients, and bilateral STN and GPi in 1 patient. Indications for DBS were motor fluctuations in 32 patients, camptocormia in 3 patients, and not specified in 61 patients. DBS configuration was double monopolar in 33 patients, monopolar in 9, bipolar in 3, and not reported in 51 patients. Other DBS parameters were variable and reported only in 7 of 21 studies (median voltage, frequency and pulse width were 2.8 V, 130 Hz, and 60 μs, respectively). Median levodopa-equivalent dopaminergic dose percentage reduction after DBS was 50.0%, and median postsurgical follow-up time was 23 months.

Outcome measures were the thoracolumbar angle in 71 patients, clinical observation in 12, item 28 of UPDRS-III in 8, item trunk of BFMDRS in 3, shoulder-hip-knee angle in 1, and not reported in 1 patient. Comparing the absolute values of these outcomes before and after DBS, it was determined that Parkinsonian camptocormia improved in 57 of 96 patients (59.4%) and remained the same or worsened in 39 of 96 patients (40.6%). The ranges of percentage change from before to after DBS were: (1) 4.3% to 100% reduction (45 patients), 2% to 100% increase (14 patients), and no change (12 patients) in thoracolumbar angle by measurement; (2) 77.8% to 100% reduction (4 patients) and not specified change (8 patients) in thoracolumbar angle by clinical observation; (3) 33.3% to 50% reduction (5 patients) or no change (3 patients) in item 28 of the UPDRS-III; (4) 25% to 33.3% reduction (2 patients) and no change (1 patient) in item trunk of the BFMDRS; and (5) 20.3% increase (improvement) in shoulder-hip-knee angle in 1 patient (from 133 to 160 degrees). Using the >30-degree thoracolumbar angle definition of camptocormia, this postural deformity resolved after DBS in 40 patients (41.7%), persisted in 34 patients (35.4%), and was undetermined in 22 patients.

Dystonic Camptocormia

Extracted data for dystonic camptocormia is summarized in Table 2. A total of 15 dystonia patients and 1 myoclonus-

TABLE 5 *Summary of DBS prognostic factors and recommendations for patients with postural deformities based on this systematic review*

Postural Deformity	Prognostic Factors for DBS	Recommendations for DBS (Low level of evidence/High risk for bias)
Camptocormia (trunk anteroflexion, T-L angle ≥30 or 45°)	Underlying disease process (dystonia, PD, neuromuscular conditions, bone/joint deformities)	• Dystonia: GPi DBS should be offered.[12,16] • PD: No evidence to treat with DBS. No evidence to compare STN vs. GPi. • Neuromuscular, bone/joint: unlikely to benefit from DBS.[8,10,13,14,20,21]
	Age and duration of underlying disease process	• Younger patients with shorter disease duration might be more likely to respond to DBS.[9,45]
	Duration of deformity	• Shorter duration (≤1.5–2.0 years) might be more likely to respond to DBS.[9,11,45]
	Response to dopaminergic therapy	• Levodopa responsive deformity might be more likely to improve after STN DBS.[9,11] • Longer disease or deformity duration might be associated with reduced L-dopa responsiveness.[9] • Dopaminergic-induced deformity might improve with dose reduction after STN DBS.
Pisa syndrome (trunk lateroflexion, lateral T-L angle ≥10°)	Underlying disease process (PD, dystonia, neuromuscular conditions, bone/joint deformities)	• PD: no evidence to treat with DBS. Unilateral PPN DBS still experimental.[26,27] • Assess for dystonic features to consider UL or asymmetric DBS.[25–27] • Probably less likely to respond if there is neuromuscular compromise or structural bone/joint deformity.
	Response to dopaminergic therapy	• No evidence for levodopa responsiveness as predictor of response to DBS. • Dopaminergic-induced deformity might improve with dose reduction after STN DBS.[2,3]
Opisthotonus (trunk retroflexion)	Underlying disease (only dystonia reported)	• Dystonia: bilateral GPi DBS should be considered.[32,33]
Anterocollis (neck anteroflexion ≥45° or C7 sagittal vertical axis > 5 cm)	Underlying disease process (PD, dystonia[1], neuromuscular conditions, bone/joint deformities)	• PD: no evidence to treat with DBS. • Dystonia: consider bilateral GPi DBS.[1] • Less likely to respond if there is neuromuscular compromise or structural bone/joint deformity[28–30]
	Response to dopaminergic therapy	• Dopaminergic-induced deformity might improve with dose reduction after STN DBS.[30]

[1] Anterocollis caused by isolated dystonia was not included in this review.
T-L, thoracolumbar; UL, unilateral.

dystonia patient treated with bilateral GPi-DBS had presurgical camptocormia, and individual data were available for all of them (10 men, 6 women). Median presurgical dystonia duration was 5 years, and median presurgical camptocormia duration was 36 months. Median age at GPi-DBS surgery was 49 years. Two patients had upper camptocormia, 5 lower camptocormia, 1 both, and the camptocormia subtype was undetermined in 8 patients. Thirteen patients had camptocormia plus other dystonic abnormalities, and 1 patient had pure lower dystonic camptocormia. Coexistence of dystonic or postural abnormalities was not specified in 2 patients.

Camptocormia was not levodopa responsive in 5 patients whereas levodopa responsiveness was not reported in 7 patients. Trunk paraspinal myopathy was not found in 5 patients (31.25%), diagnosed in 1 patient (6.25%), and not reported in 10 patients. Spinal bone deformities were not identified in the only patient for whom they were reported.

The DBS target was the bilateral GPi, and the indication for DBS was camptocormia in all patients. DBS configuration was monopolar in 7 patients, double monopolar in 1, bipolar in 4, and not reported in 4 patients. Other DBS parameters were variable and reported in 4 of 7 studies (median voltage, frequency and pulse width of 3 V, 130 Hz, and 90 μs, respectively). Median postsurgical follow-up time was 31 months.

Outcome measures were the item trunk of the BFMDRS in 10 patients, clinical observation in 5, and thoracolumbar angle in 1 patient. Comparing the absolute values of these outcomes before and after DBS, it was determined that dystonic camptocormia improved in all patients. The ranges of percentage change from before to after DBS were: (1) 50% to 100% reduction (10 patients) in item trunk of the BFMDRS; (2) 100% thoracolumbar angle reduction (1 patient) by measurement (from 90 to 0 degrees); (3) 100% thoracolumbar angle reduction (2 patients) by clinical observation (both 90 to 0 degrees); and (4) not specified clinical improvement in the remaining 3 patients. Using the >30-degree thoracolumbar angle definition of camptocormia, this postural deformity resolved after DBS in 4 patients (25%), persisted in none, and was undetermined in 12 patients.

Parkinsonian Pisa Syndrome

Extracted data for Parkinsonian Pisa syndrome is summarized in Table 3. A total of 20 PD patients treated with bilateral STN-DBS had presurgical Pisa syndrome, and 1 additional patient developed Pisa syndrome after STN-DBS.[25] Seven of the 20 patients were cases included in two of the three large studies mentioned in the Parkinsonian camptocormia section.[6,7] In one of those studies, 2 of 158 PD patients (1.27%) treated with STN-DBS for motor fluctuations had presurgical Pisa syndrome, their lateral thoracolumbar angle improved by 67.5%, and Pisa syndrome disappeared after STN-DBS.[6] In the other relatively large report, 5 of 101 PD patients (4.9%) treated with STN-DBS for motor fluctuations had presurgical Pisa syndrome. After combining these patients with those with camptocormia, it was reported that 64.3% of them improved, 32.1% remained stable, and 3.6% worsened after STN-DBS based on item 28 of the UPDRS-III.[7]

Individual data were available for 14 PD patients with Pisa syndrome (5 men, 9 women). Median presurgical PD duration was 11 years, and median presurgical deformity duration was 12 months. Median age at DBS surgery was 69 years. Direction of tilting was to the right in 3 patients whereas 1 patient had additional camptocormia, which was not specified in the remaining cases.[14] The deformity was not levodopa responsive in 10 patients, levodopa responsive in 4, and not specified in 1 patient. Evidence for trunk paraspinal myopathy was not reported in any study. Spinal bone deformities were evidenced in 8 patients, not evidenced in 4, and not reported in 3 patients.

The DBS target was the bilateral STN in 11 patients,[14,25] bilateral GPi in 1,[24] and unilateral PPN in 2 patients.[26,27] The indication for DBS was motor fluctuations in 10 patients,[14,25] Pisa syndrome in 2,[24,26] severe postural instability and falls in 1 patient,[27] and not reported in 1 patient.[14] DBS configuration was monopolar in 2 patients, bipolar in 2, and not reported in 4 patients. Other DBS parameters were significantly variable and reported in four of the five studies (median voltage, frequency, and pulse width of 4.6 V, 92.5 Hz, and 68 μs, respectively). Median postsurgical follow-up time was 12 months.

Outcome measures were item 28 of the UPDRS-III in 10 patients, lateral thoracolumbar angle in 3, and clinical observation in 1 patient. Comparing the absolute values of these outcomes before and after DBS, it was determined that Pisa syndrome improved in 10 patients (71.4%), remained stable in 3, and worsened in 1 patient. The ranges of percentage change were: (1) 33.3% to 50% reduction (7 patients) and no change (3 patients) in item 28 of the UPDRS-III and (2) 42.3% to 66.7% reduction (3 patients) in lateral thoracolumbar angle by measurement. In the remaining patient, we were unable to objectivize the clinically observed improvement. Using the >10-degree lateral thoracolumbar angle definition of Pisa syndrome, this postural deformity resolved in 1 patient after contralateral STN voltage reduction,[25] persisted in 2 patients, and was undetermined in 11 patients.

Dystonic Opisthotonus

Extracted data for dystonic opisthotonus are summarized in Table 2. A 29-year-old man with dystonic opisthotonus for 18 years significantly improved by clinical observation 4 months after bilateral GPi-DBS (right GPi: C + 0–/3.5 V/130 Hz/90 μs; left GPi: C + 4–/3.5 V/130 Hz/90 μs).[32] The trunk item of the BFMDRS improved from 12 to 2 points after bilateral GPi-DBS in another man aged 25 years with dystonic opisthotonus for 9 years (DBS mode/contacts not specified, bilateral GPi: 3.5 V/130 Hz/60 μs).[33]

Parkinsonian Anterocollis

Extracted data for parkinsonian anterocollis are summarized in Table 3. Three PD patients aged 50 to 60 years (2 women) with L-dopa-resistant anterocollis lasting for 1 to 132 months were treated with bilateral STN-DBS for motor fluctuations.[28–30] Anterocollis improved by clinical observation in 1 patient without evidence of cervical paraspinal myopathy[30] and remained the same by clinical observation in the other 2 patients (both with evidence of either paraspinal myopathy or spinal deformities). DBS mode and settings were not reported. Outcomes were based on clinical observation in all patients. Postsurgical follow-up was 6 months for 1 patient[30] and not reported for the other 2 patients.

Discussion

All 38 studies addressing the effects of DBS in postural deformities are observational and retrospective (i.e., nonrandomized and lacking a control group). Moreover, DBS was not performed to treat the postural abnormality in most patients (with the exception of dystonic camptocormia and opisthotonus). Thus, the level of evidence on this topic is of low quality and has a high risk of bias that might be further increased by the use of meta-analytical or other statistical techniques.[44] Despite these methodological constraints, we were able to identify five groups of patients with similar tendencies (Tables 1–5): (1) Parkinsonian camptocormia; (2) dystonic camptocormia; (3) Parkinsonian Pisa syndrome; (4) dystonic opisthotonus; and (5) Parkinsonian anterocollis. Of note, dystonic Pisa syndrome has not been reported as treated with DBS, and purely dystonic anterocollis was excluded from this review.

After DBS, Parkinsonian camptocormia improved in 59.4%, but persisted or worsened in 40.6% of the 96 patients with enough individual data to be analyzed in this review. Most patients were treated with STN-DBS (89 patients) versus GPi-DBS (7 patients) for motor fluctuations, but not for the camptocormia itself. Thus, there was not enough evidence to adequately compare STN and GPi as the target for parkinsonian camptocormia or any of the postural deformities included in this review, particularly because of the small sample sizes (Table 4). Five studies were recently assessed in a meta-analysis of PD patients with camptocormia who underwent STN-DBS.[45] A decrease of >50% in sagittal plane imbalance was observed in 36.4% of the 66 patients included. Interestingly, ≤2 years of camptocormia duration was reported as predictive of better outcomes with an odds ratio of 4.15. Besides camptocormia duration,[11,45] other presurgical characteristics reported as predictors of the DBS effects on camptocormia have been the camptocormia response to levodopa[9] and evidence for truncal paraspinal myopathy, including imaging-determined muscle thickness.[8,10,20,21] Given that DBS is usually used to treat motor fluctuations in these patients, reported DBS modes and settings are variable and no study has attempted to correlate specific DBS programs with changes in camptocormia.

Consistent with the relative success of GPi-DBS for patients with several types of dystonia,[46] all reported patients with dystonic camptocormia improved 50% to 100% after GPi-DBS. Even though this impressive outcome might be the result of publication bias, it is important to note that dystonic camptocormia patients were younger, had shorter disease duration, and longer camptocormia duration compared to the parkinsonian group (Table 2). As opposed to the PD patients, GPi-DBS was performed to treat dystonic camptocormia in all reported patients. Similarly, patients with dystonic opisthotonus remarkably responded to GPi-DBS. As expected when compared with STN-DBS, GPi-DBS settings for patients with dystonic camptocormia tended to require higher voltage and longer pulse width to achieve optimal therapeutic benefits.

After DBS, Parkinsonian Pisa syndrome improved by 33.3% to 66.7% in 10 of the 14 patients included in this systematic review. Most patients underwent bilateral STN-DBS for motor fluctuations, followed by bilateral GPi and unilateral PPN-DBS. No patient with dystonic Pisa syndrome and DBS was found in our search. Nevertheless, a recently reported patient with PD developed mild right-sided Pisa syndrome several years after STN-DBS.[25] This patient had some dystonic features over his right hemibody, and Pisa syndrome resolved after left-STN voltage reduction.[25] Thus, PD progression combined with detrimental DBS effects might influence the development of postural abnormalities over time. Lateralized fine-tuning of DBS settings, including significant unilateral voltage reduction, might be a therapeutic alternative for asymmetric abnormalities such as Pisa syndrome and other axial motor symptoms in PD.[25,47,48] Importantly, Pisa syndrome was the indication for bilateral GPi-DBS in 1 patient and for unilateral PPN-DBS in another patient. The PPN is still considered an experimental DBS target, but it has been observed that the beneficial effects of PPN-DBS in postural abnormalities tend to fade away over time.[26] In addition, the two studies using PPN-DBS adopted a unilateral approach targeting the side ipsilateral[26] or contralateral[27] to the bending side, which raises the question of why Pisa syndrome improved regardless of the stimulated side. PPN has extensive bilateral projections, but the contribution of a placebo response cannot be overlooked. As opposed to dystonic anterocollis, the small number of reported patients with Parkinsonian anterocollis (dropped head syndrome) had a variable response to STN-DBS performed for motor fluctuations. Yet, it appears that the presence of cervical paraspinal myopathy and/or spinal deformities might influence the postsurgical outcome in these patients.

This review has several limitations. As previously mentioned, we decided not to perform meta-analytical techniques given the low quality of available evidence, relatively small sample sizes, and the possibility of further contributing to publication bias. In this regard, the semiquantitative data description presented in this review is intended to be a summary of the available evidence and not true data analysis. Another potential limitation is that the exclusion of anterocollis caused by isolated dystonia might have resulted in the very small number of patients with anterocollis included in this review. Patients with dystonic anterocollis without PD have been studied in DBS trials for cervical dystonia, but it is important to note that Parkinsonian anterocollis might have dystonic features as well. Given that this distinction might not be possible even after careful clinical and electrophysiological assessment, we thought it would be more useful to focus on PD patients without clearly reported evidence for dystonia.

Conclusion

The currently available scientific literature on the effects of DBS in postural abnormalities has low quality and high risk for bias. Nonetheless, careful clinical and possibly electrophysiological assessment of dystonic features seems to be particularly relevant given that bilateral GPi-DBS has been consistently reported as associated with significant improvements in dystonic camptocormia and dystonic opisthotonus. Patients with Parkinsonian camptocormia, Pisa syndrome, and/or anterocollis have been reported as treated with bilateral STN, bilateral GPi, and unilateral PPN-DBS for other indications, such as motor fluctuations, and they have more variable responses. There is not enough evidence to adequately compare STN and GPi as DBS targets for the treatment of Parkinsonian camptocormia. However, patients with PD who have significant treatment-resistant postural deformities with dystonic features might benefit from GPi-DBS. Table 5 summarizes DBS prognostic factors and therapeutic recommendations for patients with postural deformities based on this systematic review. Proper prospective and randomized trials are needed in order to confirm these trends.

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Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

K.J.L.: 1A, 1B, 1C, 2A, 2B, 3A

A.F.: 1A, 1B, 1C, 2A, 2B, 2C, 3B

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